REMARKS

Claims 1-11 and 16 are pending. Non-elected claims 12-15 have been cancelled. Applicants hereby reserve the right to file a divisional application directed to this non-elected subject matter.

Claims 1-11 have been amended. No new matter has been added by way of the above amendments. For instance, the claims have been amended to recite an "isolated or purified" peptide. Also, the claims have been amended to remove reference to the term "fragment", "fragments", or "series of peptide." Claims 1 and 2 have been amended to recite that the peptide or partial sequence of the peptide has cell-death inhibitory activity. Claims 6, 8 and 9 have been amended to remove the phrase "protecting from exacerbation of conditions of." Lastly, new claim 16 is supported by originally filed claim 7. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Objection to the Drawings

The Examiner has objected to the drawings asserting that Figure 2 is not present. Applicants traverse and submit that Figure 2 was originally filed with the present application on May 18, 2001. As evidence that the USPTO received this Figure 2,

Applicants have attached hereto a date receipt postcard which indicates that a total of 10 Drawing Sheets were submitted and received. Applicants also attached a replacement copy of Figure 2. The Examiner is requested to make this replacement copy a part of the record.

Issues under 35 USC § 101

The Examiner has rejected claims 1-11 under 35 U.S.C. § 101. Applicants traverse this rejection and submit that the claims have been amended to recite an "isolated or purified" peptide, as suggested by the Examiner. Reconsideration and withdrawal of this rejection are requested.

Issues under 35 USC § 112, second paragraph

The Examiner has rejected claims 1-11 under 35 U.S.C. § 112, second paragraph for the reasons recited at pages 3-4 of the outstanding Office Action. Applicants respectfully traverse each of these rejections.

First, the Examiner asserts that the term "fragments" or "fragment" is unclear. Applicants traverse and submit that this language has been removed from the relevant claims.

Second, the Examiner asserts that the phrase "series of peptides" is unclear. Applicants traverse and submit that this language has been removed from the relevant claims.

Third, the Examiner asserts that the phrase "partial sequence" is unclear. In particular, the Examiner asserts that the phrase includes anything other than the full length sequence, or which a deletion, truncation, or substitution of one or more amino acids could constitute a "partial sequence." Applicants traverse this rejection. Although this claim term may arguably be broad, it is not indefinite.

Applicants respectfully submit that the second paragraph of 35 USC § 112, requires that the claims particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Nowhere within the statute is there an explicit recitation that the scope of the claim, whether it is broad or narrow, adversely effects the distinctness of the claimed subject matter. Furthermore, the MPEP states,

> Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph. (see MPEP 2173.04).

As such, Applicants respectfully submit that the rejection of the phrase "partial sequence" under 35 U.S.C. § 112, second paragraph is improper.

Fourth, the Examiner asserts that the phrase "wherein Xaa is selenocysteine, or having a partial sequence of these amino acid

sequences" is unclear. Applicants traverse and submit that is phrase has been amended to recite "wherein Xaa is selenocysteine, or a partial sequence of the amino acid sequence having cell death inhibitory activity of the amino acid sequences of formulas (I) or (II)." Accordingly, this rejection is moot.

Fifth, the Examiner asserts that the phrase "protecting" is unclear. Applicants traverse and submit that this language has been removed from the relevant claims.

Sixth, the Examiner asserts that the phrase "cells of the immune system are involved" is unclear. Applicants traverse and submit that this language has been amended to recite "the immune system is involved." Accordingly, this rejection is moot.

Seventh and lastly, the Examiner asserts that the term "estimating" is unclear. Applicants disagree with the Examiner. The present specification teaches estimation techniques for determining cell death inhibition, for instance, the Examiner is referred to the paragraph at page 9, line 17 to page 10, line 7 of the present specification. Additional description is found at page 10, line 23 to page 11, line 7. Even more specific discussion concerning the estimation of the activity to cell death inhibition is found in the present specification, for instance in Example 1 (assay) at page 28, line 17 to page 29, line 15. Accordingly, in view of the teaching in the present specification, one of ordinary

skill in the art would have no problem in understanding the term "estimating" as it is used in the present claims.

In summary, Applicants submit that the present claims define subject matter which is fully definite as required by 35 USC § 112, second paragraph. Reconsideration and withdrawal of these rejections are therefore requested.

Issues under 35 USC § 112, first paragraph (written description)

The Examiner has rejected claims 1-11 under 35 U.S.C. 112, first paragraph for the reasons recited at pages 4-6 of the outstanding Office Action. The Examiner asserts that the application only describes SEQ ID NOS: 1 and 2 and therefore concludes that there is no written description for a series of peptide fragments or variants of SEQ ID NOS: 1 and 2 wherein there are deletions, substitutions or additions of amino acids. Applicants respectfully disagree with the Examiner.

Applicants submit that the present specification contains a sufficient written description of the subject matter as claimed. As such, one having ordinary skill in the art would understand that Applicants were in possession of the subject matter as claimed at the time of filing the application.

The present specification does not recite only SEQ ID NOS: 1 and 2 as asserted by the Examiner. In fact, several other structural aspects of the invention are discussed and claimed. For

instance, the peptides or partial sequences must have "cell death-inhibitory activity." Also, the specification, at page 7, discloses other structural aspects of peptides. For instance, these sequences are recovered in fractions of molecular weight 10 kDa to 30 kDa by molecular size fractionation with membrane. These sequences also have structures showing isoelectric points at between pH 7 and pH 8 and at pH 8 or more in blood as a result of testing of binding to ion exchange resin. The sequences also show two bands at molecular weight 13 to 14 kDa and two bands at 16 to 17 kDa, the latter being a glycosylated form of the former, in non-reductive SDS-PAGE. Moreover, the sequences have a band patter of 3 to 4 kDa, 7 to 9 kDa and 10 to 12 kDa in SDS-PAGE under reductive conditions in addition to the bands described above.

Accordingly, the amount of structural information provided by the present specification is not limited to only SEQ ID NOS: 1 and 2 as asserted by the Examiner. Also, Applicants are not only claiming a series of peptides or a partial sequence of a peptide. In fact, the present claims require that the isolated or purified peptide or partial sequence thereof have "cell death-inhibitory activity". Additionally, the peptide or partial sequence thereof must also comprise the amino acid sequence consisting of 103 amino acid residues at the C-terminal of selenoprotein P, or having said sequence with one or several amino acid residues therein being

deleted, substituted or added. Thus, not only do the claims recite specific structure, but they also require the corresponding function of cell-death inhibitory activity.

Accordingly, Applicants submit that sufficient structure and corresponding function are recited in the present claims such that there exists sufficient written. The Examiner is therefore requested to withdraw this rejection.

Issues under 35 USC § 112, first paragraph (enablement)

The Examiner has rejected claims 1-11 under 35 USC § 112, first paragraph for the reasons recited at pages 6-10 of the outstanding Office Action. Applicants respectfully traverse.

The Examiner asserts that the specification does not provide sufficient teaching of how to make and how to use fragments, series of fragments or variants of selenoprotein P that is used as a medicament for preventing or treating disease related to cell death in an in vivo system. Applicants disagree with the Examiner.

The present specification discloses a myriad of purification techniques at page 11, lines 8-25 for selenoprotein P. Then, in Example 2, there is a description of a detailed method of purification culminating in an increase in specific activity of the product of about 5000 to about 10000 times.

Also, the present specification provides a method to screen the purified product for cell death-inhibitory activity. The

Examiner is referred to page 19, line 8 to page 20, line 15 as well as the Examples. Screening of potentially active peptides may be labor intensive, but does not constitute undue experimentation.

In summary, selenoprotein P has a known amino acid sequence (see page 18,lines 9-18 of the present specification). Applicants are simply claiming a specific portion of this sequence which retains cell death-inhibitory activity. The specification contains a detailed procedure for obtaining candidate peptides as well as a method for screening these peptides for activity. Therefore, Applicants submit that the presently claimed subject matter is fully enabled by the present specification. Reconsideration and withdrawal of this rejection are therefore requested.

Issues under 35 USC § 102(b)

The Examiner has rejected claims 1, 5, 6 and 10 under 35 USC § 102(b) as being anticipated by Rafferty (*Biochem. J.*, 1998 May 15; 332(Pt1): 231-6). Applicants respectfully traverse.

Rafferty discloses that human skin cells are protected from UVB-radiation-induced cell death by adding selenium. The "selenium" disclosed by Rafferty is "selenite" or "selenomethionine", but not "selenoprotein P". Thus, while the present invention deals with selenoprotein P, this is not the subject matter of the Rafferty reference.

Rather, Rafferty explains that selenium exerts its protecting activity not by a direct antioxidant chemical action, but through incorporation into selenoproteins. The selenoproteins of approximately 10 to 60 kDa are synthesized within cells and Rafferty attempts to elucidate the mechanism through which protective activity occurs. Rafferty concludes that "[t]he susceptibility of a cell to UVB-induced damage will depend on the total expression of a wide range of antioxidant enzymes and DNA repair mechanisms, and not necessarily on difference in the expression of a single specific selenoprotein." See page 235, right hand column, second full paragraph of Rafferty.

Applicants note that although selenoprotein may be synthesized within cells, Rafferty never discloses or suggests selenoprotein P much less a fragment thereof. Moreover, a variety of selenoproteins of 10 to 20 kDa were separated by SDS-PAGE. However, none of these could be fragments of selenoprotein P since fragmentation can occur after secretion out of cells.

In summary, Rafferty concerns a totally different art from the presently claimed subject matter. Therefore, no anticipation exists based upon Rafferty. Reconsideration and withdrawal of this rejection are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Marc Weiner (Reg. No. 32,181) at the telephone

number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), Applicant hereby petitions for an extension of three (3) months to June 18, 2003 in which to file a reply to the Office Action. The required fee of $930.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

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MSW/CAM/mmi
0020-4867P

Attachment: Replacement copy of Figure 2
Date stamped postcard receipt